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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,177	12/15/2004	David Bonnaffe	10404.004.00-US	5723

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EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,177	BONNAFFE ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40 and 42-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18-23* is/are allowed.

6)☒ Claim(s) *1-17, 24-40 and 42-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 2/15/2008 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claim 41 has been canceled.

2. New Claims 44-50 have been added.

3. Claims 1, 3, 6, 18, 24-28, 32-34, 36-37 and 42-43 have been amended.

4. Remarks drawn to claim objections and rejections under 35 USC 101, 112, first and second paragraphs and 103.

Claims 1-40 and 42-50 are pending in the case.

The objections to Claims 24-28 and 41 have been overcome by amendments. The objection to claims 36-39 is being maintained for reasons of record. Claims 36-39 are still seen as duplicates of claim 35. Claims 42-43 are objected to because of the following informalities: Claim 43 is a duplicate of claim 42. Appropriate correction is required.

The rejection of Claims 25, 32-34 and 42-43 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101, has been overcome by amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 27-34, 38-40, 43 and 45-46 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compound of formula (I) and the process of making it, does not reasonably provide enablement for the use of the said compounds in the treatment of the diseases and prevention of transplant rejection as recited in the instant claims, is being maintained for reasons of record.

Applicants have traversed the rejection arguing that:

The specification provides the medicaments containing the compound (or compounds) (I) alone can be administered at doses which can eb determined beforehand by means of routine experimentation, according in particular to the desired effect and doses may range from 0.1 to 200mg per individual per day.

Applicants' arguments are not found to be persuasive. Applicants have not provided substantive arguments. Just arguing that the dosage is provided in the specification is not seen sufficient to overcome the rejection. No arguments have been advanced as to why the methods of treatment as instantly claimed are enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 8, 30-31 and 39-40 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention, is being maintained for reasons of record. Claims 8, 30-31 and 39-40 still recite the phrase "for example"

The rejection of Claims 3, 6, 18, 25, 27, 30, 32-34 and 42-43 has been overcome by amendment.

The following new rejections are made of record necessitated by amendment.

Claims 25, 32-34 and 42-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25, 32-34 and 42-43 are drawn to a method of preparing a medicament but do not recite any positive steps for the same. In the absence of steps for the said method of preparation the claims are rendered indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of Claims 1-17 and 24-40 and 42-50 under 35 U.S.C. 103(a) as being unpatentable over Lorat-Jacob (WO 97/03700, English Translation; Document B1 in IDS of 03/04/2005) in view of Morel et al (Cytokine, 1996, 8(7), 557-566; Document C2 in IDS of 03/04/2005) and Turnbull et al (WO 93/19096), is being maintained for reasons of record.

Applicants have traversed the rejection by arguing that:

1. Lorat-Jacob dopes not exemplify the compound of instant formula (I).

2. Turnbull teaches that heparin and heparan sulfate with the complexity and heterogeneity with large number of different disaccharide units may have different activities and have undesired side effects and would lack specificity in binding to growth factors on cell surfaces. There is no suggestion to make the fragments A and B in the instant formula symmetrical.

3. The glucosamine in instant formula (I) in claim 1 does not have s sulfate group at the 3-position. Lorat-Jacobs does not teach or suggest this feature.

Applicants' arguments are not found to be persuasive.

According to Lorat-Jacob, the agent of his invention contains the groups A and B, which may or may not be similar. The fact that it may be similar is a suggestion that the compounds of instant formula (I) can be symmetrical (by being the same). The oligosaccharide groups can contain a percentage of sulfate or phosphate groups that is sufficient to confer affinity for gamma interferon (page 8, lines 1-3). The anticoagulant activity of heparin is well known to one of skill in the art. Hence, the skilled artisan would adjust the percentage and distribution of the sulfate groups in order to avoid the anticoagulant drawbacks.

Morel et al, drawn to γ-interferon and the role of heparan sulfate, teach that the concept that cytokine and growth factor activity is governed not only by their bindings to specific cell surface receptors, but also to extracellular components is well accepted and that the interaction of γ-interferon with heparan sulfate/heparin-like molecules result in a tight control of the cytokines (page 564, right column, first full paragraph). This teaching of Morel and the teaching of Lorat-Jacob as explained above, suggests to one of ordinary skill in the art that saccharide oligomers that have heparin or heparan sulfate monomeric units comprising glucosamine units and glucuronic acid units are important for binding to cytokines like γ-interferon in order to modulate their activity.

Turnbull et al, drawn to oligosaccharides, teaches that heparin or heparan sulfate with the complexity and heterogeneity with a large number of different disaccharide units may have different activities and have undesirable side effects and would lack specificity in binding to growth factors on cell surfaces. What is needed is a substantially homogenous preparation of a relatively small molecular compound (page 4, line 38 through page 5, line 13). This means that

the structure of the saccharide units in heparin or heparan sulfate should be same or uniform for reducing the side effects and increasing the beneficial activity, i.e., binding to cytokines like γ-interferon by heparin and heparan sulfate fragments that are extracellular components (as taught by Morel above). Hence this is a suggestion to make fragments A and B in the compounds of Lorat-Jacob uniform or symmetrical so that the binding to γ-interferon is the main reaction that takes place and not any other side reaction that is not beneficial. Lorat-Jacob also suggests that in their compound A-X-B, the fragments A and B may be similar (Lorat-Jacob, page 7, lines last three lines). Both Lorat-Jacob and Turnbull suggest having a symmetrical sturcutre.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make compounds of instant formula (I) and their compositions and complexes with γ-interferon as a medicament for modulating the activity of γ-interferon and thereby treatment of cancers and infectious diseases of viral, bacterial or parasitic origin (Lorat-Jacob page 13, first full paragraph) since such is seen to be taught in the prior art using closely analogous compounds.

Conclusion

1. Claims 1-17, 24-40 and 42-50 are rejected

2. Claims 18-23, drawn to a process for preparing a compound of formula (II) is seen to be free of prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

GK